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Gene therapy superior to half-matched transplant for 'bubble boy disease'

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New research published online today in *Blood*, the Journal of the American Society of Hematology (ASH), reports that children with "bubble boy disease" who undergo gene therapy have fewer infections and hospitalizations than those receiving stem cells from a partially matched donor. The research is the first to compare outcomes among children with the rare immune disorder - also known as X-linked severe combined immunodeficiency (SCID-X1) - receiving the two therapeutic approaches.

Children with SCID-X1 are born with a genetic defect that prevents them from developing a normal immune system. Because they are prone to life-threatening infections, infants with SCID-X1 must be kept in a sterile, protective bubble and require extensive treatment for survival beyond infancy. Infants with SCID are most likely to survive if they receive a stem cell transplant from a fully matched donor - typically a sibling - a procedure that replaces an infant's diseased stem cells with healthy donor cells. Following a successful fully matched transplant, infants with SCID-X1 are able to produce their own immune cells for the first time.

In the absence of a fully matched stem cell donor, infants with SCID-X1 may receive a transplant from a partial, or "half-matched," donor - typically their mother or father. They may also undergo gene therapy, a much different approach. Gene therapy for SCID-X1 involves extracting an infant's own bone marrow, using a virus to replace faulty genetic material with a correct copy, and then giving "corrected" bone marrow

back to the patient. Half-matched stem cell transplant and gene therapy represent secondary treatment approaches for infants with SCID-X1. Until recently, researchers had not yet compared outcomes among children treated with each respective approach.

"Over the last decade, gene therapy has emerged as a viable alternative to a partial matched stem cell transplant for infants with SCID-X1," said lead study author Fabien Touzot, MD, PhD, of Necker Children's Hospital in Paris. "To ensure that we are providing the best alternative therapy possible, we wanted to compare outcomes among infants treated with gene therapy and infants receiving partial matched transplants."

Dr. Touzot and colleagues studied the medical records of 27 children who received either partial-matched transplant (13) or gene therapy (14) for SCID-X1 at Necker Children's Hospital between 1999 and 2013. The children receiving half-matched transplants and the children receiving gene therapy had been followed for a median of six and 12 years, respectively.

The researchers compared immune, or T-cell, development among patients and also compared key clinical outcomes such as infections and hospitalization. Investigators observed that the 14 children in the gene therapy group developed healthy immune cells faster than the 13 children in the half-matched transplant group. In fact, in the first six months after therapy, T cell counts had reached normal values for age in more than three-fourths (78%) of the gene therapy patients, compared to roughly one-fourth (26%) of the transplant group. The more rapid growth of the immune system in gene therapy patients was also associated with faster resolution of some opportunistic infections (11 months in gene therapy group vs. 25.5 months in half-matched transplant group). These patients also had fewer infection-related hospitalizations (3 in gene therapy group vs. 15 in half-matched transplant group).

"Our analysis suggests that gene therapy can put these incredibly sick children on the road to defending themselves against infection faster than a half-matched transplant," Dr. Touzot said. "These results suggest that for patients without a fully matched stem cell donor, gene therapy is the next-best approach."

Provided by American Society of Hematology